UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

August 9, 2011

MEMORANDUM

Subject:	Name of Pesticide Product:	Hartz Ref #132	
	EPA File Symbol:	2596-RAT	
	DP Barcodes:	D388559	
	Decision No.:	445859	
	Action Code:	R310	
	PC Codes:	128965	Ethofenprox
		067501	Piperonyl butoxide
		057001	MGK 264

From: Breann Hanson, Biologist
Technical Review Branch (TRB)
Registration Division (RD; 7505P)

To: Bonaventure Akinlosotu, RM Team 10
Insecticide Branch
Registration Division (7505P)

Applicant: The Hartz Mountain Corporation
400 Plaza Drive
Secaucus, New Jersey 07094-3688

FORMULATION FROM LABEL:

Active Ingredient:			% by wt
128965	Ethofenprox	CAS No. 80844-07-1	55.0
067501	Piperonyl butoxide	CAS No. 51-03-6	10.0
057001	MGK 264	CAS No. 1113-48-4	1.0
Other Ingredients:			34.0
		Total:	100.0%

ACTION REQUESTED: The Risk Manager requests: "For your review: MRID Nos. 484058-01, 02, 03, 04, 05 for an R310. N/B: Same data pkg/studies applicable to 2596-RAT, RAI & RAO."

BACKGROUND: The Hartz Mountain Corporation (herein the "registrant") has submitted acute oral (MRID 484058-02), acute dermal (MRID 484058-03), primary eye irritation (MRID 484058-05), primary dermal irritation (MRID 484058-04), and dermal sensitization (MRID 484058-01) studies in support of their proposed product, Hartz Ref#132, EPA File Symbol: 2596-RAT. The studies were performed at Eurofins|Product Safety Laboratories (PSL), Dayton, New Jersey, US. The registrant is requesting a waiver from the acute inhalation toxicity data requirement.

COMMENTS AND RECOMMENDATIONS:

1. All five studies have been reviewed and all are classified as Acceptable. Acute inhalation studies are not required for pet spot-on products (per previous reviews authored by B. Backus); therefore, the waiver is granted. The product will be placed into Acute Toxicity Category IV for acute inhalation.

2. Both test substances (Hartz Dermal Treatment (Sample #13346) and Hartz Dermal Treatment -D (Sample #13327)) evaluated by Eurofins|PSL in the studies reviewed herein contained, according to information provided within the study reports: 55% Etofenprox, 10% Piperonyl butoxide, 1% N-octyl bicycloheptene dicarboximide (MGK 264), as well as 2.3% Methoprene and 1% Nylar. As noted in the CSF and label for the proposed product, 2596-RAT, Hartz is proposing to register a product that contains only Etofenprox, Piperonyl butoxide and MGK 264, at the tested concentrations. Although the tested formulation is not the same formulation being marketed as 2596-RAT, TRB would not expect the reduced concentration of total active ingredients (AIs) and the complete deletion of 2 AIs from the formulation to increase the toxicity of 2596-RAT. TRB would also not expect the replacement of 2 AIs with cleared inerts of low toxicity to increase the toxicity of 2596-RAT. Therefore, the formulation tested in the studies reviewed herein may be applied to the registration of 2596-RAT.

3. The acute toxicity profile for Hartz Ref#132, EPA File Symbol: 2596-RAT, is as follows:

Acute oral toxicity	IV	Acceptable	MRID 48405802
Acute dermal toxicity	IV	Acceptable	MRID 48405803
Acute inhalation toxicity	IV	WAIVED	
Acute eye irritation	III	Acceptable	MRID 48405805
Primary skin irritation	III	Acceptable	MRID 48405804
Dermal sensitization	Negative	Acceptable	MRID 48405801

4. Based on the toxicity profile above, the following are the precautionary and first aid statements for this product as obtained from the Label Review System:

PRODUCT ID #: 002596-00167
PRODUCT NAME: Hartz Ref#132

PRECAUTIONARY STATEMENTS

SIGNAL WORD: CAUTION

Hazards to Humans and Domestic Animals: Avoid contact with eyes, skin or clothing. Causes moderate eye irritation. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. [Wear protective eyewear.]*

First Aid:

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

* Protective eyewear may be specified, if deemed appropriate.

5. The Label Review Manual has recently been updated to include the phrase (change in *italics*): "Wash thoroughly with soap and water after handling..., using tobacco *or using the toilet*"; please advise the registrant of this change. The proposed label contains the appropriate signal word. TRB notes that the proposed label does not contain Toxicity Category III precautionary or first aid label language for dermal irritation; according to the above acute toxicity profile, this language should be added to the label. Based on the proposed use pattern (a dermal application to the skin of dogs and puppies) TRB acknowledges why this language was omitted.

6. The basic and any alternate CSFs for the product must be approved by the TRB Product Chemistry Team.

Reviewer: Breann Hanson **Date:** August 9, 2011
Risk Manager (EPA): Bonaventure Akinlosotu, RM 10

STUDY TYPE: Acute Oral Toxicity - Rat; OPPTS 870.1100; OECD 425

TEST MATERIAL: Hartz Dermal Treatment (Sample #13346) (Etofenprox: 55%, Piperonyl butoxide: 10%, N-octyl bicycloheptene dicarboximide: 1%, Methoprene: 2.3%, Nylar: 1%; EPSL Reference Number 091204-1R; clear slight yellow tint liquid)

CITATION: Durando, J. (2010) Acute Oral Toxicity Up and Down Procedure in Rats of Hartz Dermal Treatment (Sample #13346). Eurofins PSL No.: 28782. Unpublished study prepared by Eurofins|PSL. March 5, 2010. MRID 48405802.

SPONSOR: The Hartz Mountain Corporation

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 48405802), three fasted, female rats (age: 9-10 weeks; weight: 183-194 g; source: Ace Animals, Inc., Boyertown, PA; strain: Sprague-Dawley derived, albino) were given a single oral gavage dose of Hartz Dermal Treatment (Sample #13346) (Etofenprox: 55%, Piperonyl butoxide: 10%, N-octyl bicycloheptene dicarboximide: 1%, Methoprene: 2.3%, Nylar: 1%; EPSL Reference Number 091204-1R; clear slight yellow tint liquid) at a limit dose of 5000 mg/kg bw. Body weights were recorded prior to dosing (day 0) and again on days 7 and 14. Animals were observed for mortality, signs of gross toxicity, and behavioral changes during the first several hours post-dosing and at least once daily thereafter for 14 days or until death. All animals were necropsied at study termination.

All animals survived and gained body weight during the study period. Post-dosing, all 3/3 animals were hypoactive and exhibited ano-genital staining, hunched posture and/or reduced fecal volume; animals recovered by Day 4 and appeared active and healthy for the remainder of the 14-day study period. No gross lesions were observed at necropsy.

LD_{50} Females > 5000 mg/kg bw

Based on the observed acute oral LD_{50} in females, Hartz Dermal Treatment (Sample #13346) is in EPA Toxicity Category IV.

This acute oral study is classified as Acceptable. It satisfies the guideline requirement for an acute oral study (OPPTS 870.1100; OECD 425) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Individual animals were dosed as follows:

Limit Test

Dosing Sequence	Animal No.	Dose level (mg/kg)	Short-Term Outcome	Long-Term Outcome
1	3101	5000	S	S
2	3102	5000	S	S
3	3103	5000	S	S

S = survival

Initially, a single animal was dosed at 5000 mg/kg; due to the absence of mortality, two additional animals were dosed at 5000 mg/kg bw, simultaneously.

Statistics: As all animals survived at a limit dose of 5000 mg/kg bw, no statistical analysis is required.

A. Mortality: None.

B. Clinical observations: All animals gained body weight during the study period. Post-dosing, all 3/3 animals were hypoactive and exhibited ano-genital staining, hunched posture and/or reduced fecal volume; animals recovered by Day 4 and appeared active and healthy for the remainder of the 14-day study period.

C. Gross Necropsy: No gross lesions were observed at necropsy.

D. Reviewer's Conclusions: In agreement with the study author, the acute oral LD_{50} for females is greater than 5000 mg/kg bw. This places the test material in EPA Toxicity Category IV.

E. Deficiencies: None.

Reviewer: Breann Hanson **Date:** August 9, 2011
Risk Manager (EPA): Bonaventure Akinlosotu, RM 10

STUDY TYPE: Acute Dermal Toxicity - Rat; OPPTS 870.1200; OECD 402

TEST MATERIAL: Hartz Dermal Treatment (Sample #13346) (Etofenprox: 55%, Piperonyl butoxide: 10%, N-octyl bicycloheptene dicarboximide: 1%, Methoprene: 2.3%, Nylar: 1%; EPSL Reference Number 091204-1R; clear slight yellow tint liquid)

CITATION: Durando, J. (2010) Acute Dermal Toxicity Study in Rats of Hartz Dermal Treatment (Sample #13346). Eurofins PSL Study No. 28783. Unpublished study prepared by Eurofins|PSL. March 5, 2010. MRID 48405803.

SPONSOR: The Hartz Mountain Corporation

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 48405803), a group of five male and five female rats (age: 9-10 weeks; weight: 293-330 g males, 206-241 g females; source: Ace Animals, Inc., Boyertown, PA; strain: Sprague-Dawley derived, albino) was dermally exposed to Hartz Dermal Treatment (Sample #13346) (Etofenprox: 55%, Piperonyl butoxide: 10%, N-octyl bicycloheptene dicarboximide: 1%, Methoprene: 2.3%, Nylar: 1%; EPSL Reference Number 091204-1R; clear slight yellow tint liquid) at a limit dose of 5000 mg/kg bw for 24 hours. The doses were applied to clipped application sites (~10% of the body surface area), covered by a 2 inch by 3 inch 4-ply gauze pad and secured with tape. After 24 hours, the test sites were gently cleansed of residual test substance. Body weights were recorded prior to dosing (day 0) and again on days 7 and 14. Animals were observed for mortality, signs of gross toxicity, and behavioral changes during the first several hours post-dosing and at least once daily thereafter for 14 days. All animals were necropsied at study termination.

All animals survived the study period. Post-application, 3/5 female animals exhibited ano-genital staining; animals recovered by Day 4 and appeared active and healthy for the remainder of the study period. Dermal irritation (erythema) was noted at 1/5 female dose sites between Days 2-6. One female animal lost a slight amount of weight (2 g) during the first week of the study period; all animals exceeded their initial body weights at study termination. No gross lesions were observed at necropsy.

LD_{50} Males > 5000 mg/kg bw
LD_{50} Females > 5000 mg/kg bw
LD_{50} Combined > 5000 mg/kg bw

Based on the observed acute dermal LD_{50}, Hartz Dermal Treatment (Sample #13346) is in EPA Toxicity Category IV.

This acute dermal study is classified Acceptable. It does satisfy the guideline requirement for an acute dermal study (OPPTS 870.1200; OECD 402) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Dose (mg/kg bw)	Mortality/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

Statistics: As all animals survived at a limit dose of 5000 mg/kg bw, no statistical analysis is required.

A. Mortality: There were no deaths.

B. Clinical observations: Post-application, 3/5 female animals exhibited ano-genital staining; animals recovered by Day 4 and appeared active and healthy for the remainder of the study period. Dermal irritation (erythema) was noted at 1/5 female dose sites between Days 2-6. One female animal lost a slight amount of weight (2 g) during the first week of the study period; all animals exceeded their initial body weights at study termination.

C. Gross Necropsy: No gross lesions were observed at necropsy.

D. Reviewer's Conclusions: In agreement with the study author, the acute dermal LD_{50} is greater than 5000 mg/kg bw. This places the test material in EPA Toxicity Category IV.

E. Deficiencies: None.

Reviewer: Breann Hanson **Date:** August 9, 2011
Risk Manager (EPA): Bonaventure Akinlosotu, RM 10

STUDY TYPE: Primary Eye Irritation - Rabbit; OPPTS 870.2400; OECD 405

TEST MATERIAL: Hartz Dermal Treatment - D (Sample #13327) (Etofenprox: 55%, Piperonyl butoxide: 10%, N-octyl bicycloheptene dicarboximide: 1%, Methoprene: 2.3%, Nylar: 1%; EPSL Reference Number 091002-2H; clear slight yellow tint liquid)

CITATION: Durando, J. (2010) Primary Eye Irritation of Hartz Dermal Treatment – D (Sample #13327). Eurofins|PSL Study No. 28363. Unpublished study prepared by Eurofins|PSL. December 9, 2009. MRID 48405805.

SPONSOR: The Hartz Mountain Corporation

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 48405805), 0.1 mL of Hartz Dermal Treatment - D (Sample #13327) (Etofenprox: 55%, Piperonyl butoxide: 10%, N-octyl bicycloheptene dicarboximide: 1%, Methoprene: 2.3%, Nylar: 1%; EPSL Reference Number 091002-2H; clear slight yellow tint liquid)was instilled into the conjunctival sac of the anesthetized right eye of three female young adult rabbits (source: Robinson Services, Inc., Clemmons, NC; strain: New Zealand albino). The upper and lower lids were held shut for approximately one second. Eyes were scored for ocular irritation according to the Draize method at 1, 24, 48, and 72-hours post-instillation. Fluorescein staining was done at 24 hours, and as needed thereafter. The anesthetized but otherwise untreated left eye of each animal served as a control.

Apart from the eye irritation noted, animals appeared active and healthy throughout the study period. No corneal opacity or iritis was observed in any treated eye during the study. One hour post-instillation, all 3/3 treated eyes exhibited "positive" grade conjunctivitis. No "positive" grade irritation was observed at 48-hours. All treated eyes were free of irritation within 72-hours. The maximum mean total score (MMTS) was 9.3, observed at 1-hour post-instillation.

In this study, the formulation is mildly irritating; Hartz Dermal Treatment - D is classified as EPA Toxicity Category III for primary eye irritation.

This study is classified as Acceptable. It does satisfy the guideline requirement for a primary eye irritation study (OPPTS 870.2400; OECD 405) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Observations	Number "positive"/number tested			
	Hours			
	1	24	48	72
Corneal Opacity	0/3	0/3	0/3	0/3
Iritis	0/3	0/3	0/3	0/3
Conjunctivae:				
Redness*	3/3	2/3	0/3	0/3
Chemosis*	0/3	0/3	0/3	0/3
Discharge**	3/3	0/3	0/3	0/3
Severity of Irritation: Mean Total Score	9.3	6.7	2.7	0.0

*Score of 2 or more required to be considered "positive."
** Not considered a positive irritation effect.

A. Observations: No corneal opacity or iritis was observed in any treated eye during the study. One hour post-instillation, all 3/3 treated eyes exhibited "positive" grade conjunctivitis (redness: score 2). No "positive" grade irritation was observed at 48-hours. All treated eyes were free of irritation within 72-hours.

B. Results: The MMTS was 9.3, observed at 1-hour post-instillation.

C. Reviewer's conclusions: In agreement with the study author; the test material is mildly irritating to the eye and is classified as EPA Toxicity Category III for primary eye irritation.

D. Deficiencies: None.

Reviewer: Breann Hanson **Date:** August 9, 2011
Risk Manager (EPA): Bonaventure Akinlosotu, RM 10

STUDY TYPE: Primary Dermal Irritation - Rabbit; OPPTS 870.2500; OECD 404

TEST MATERIAL: Hartz Dermal Treatment (Sample #13346) (Etofenprox: 55%, Piperonyl butoxide: 10%, N-octyl bicycloheptene dicarboximide: 1%, Methoprene: 2.3%, Nylar: 1%; EPSL Reference Number 091204-1R; clear slight yellow tint liquid)

CITATION: Durando, J. (2010) Primary Skin Irritation Study in Rabbits of Hartz Dermal Treatment (Sample #13346). Eurofins|PSL Study No: 28784. Unpublished study prepared by Eurofins|PSL. March 5, 2010. MRID 48405804.

SPONSOR: The Hartz Mountain Corporation

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 48405804), three female young adult rabbits (source: Robinson Services, Inc., Clemmons, NC; strain: New Zealand albino) were dermally exposed to 0.5 mL of Hartz Dermal Treatment (Sample #13346) (Etofenprox: 55%, Piperonyl butoxide: 10%, N-octyl bicycloheptene dicarboximide: 1%, Methoprene: 2.3%, Nylar: 1%; EPSL Reference Number 091204-1R; clear slight yellow tint liquid) for 4 hours. The doses were applied to intact, clipped, application sites, covered by a 4-ply, 1-inch by 1-inch gauze pad and wrapped with semi-occlusive tape. After 4 hours, the test sites were gently cleansed of any residual test substance. The animals were observed within 30-60 minutes and at 24, 48, and 72 hours and again on days 7, 10 and 14 post-gauze removal; any irritation at the dose sites was scored according to Draize.

Apart from the skin irritation noted, animals appeared active and healthy throughout the study period. Within 1-hour post-patch removal, all 3/3/ treated sites exhibited well-defined erythema (score 2) and slight edema (score 2). The overall incidence and severity of irritation decreased gradually with time. Irritation cleared from all treated sites within 14 days. The Primary Dermal Irritation Index (PDII) = 3.2.

In this study, the formulation is a moderate irritant. Based on the moderate irritation noted at the 72-hour observation, Hartz Dermal Treatment is classified as EPA Toxicity Category III for primary dermal irritation.

This study is classified as Acceptable. It does satisfy the guideline requirement for a primary skin irritation study (OPPTS 870.2500; OECD 404) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

INDIVIDUAL SKIN IRRITATION SCORES [ERYTHEMA/EDEMA]

Animal No.	Sex	Hours after patch removal				Days after patch removal		
		I	24	48	72	7	10	14
3501	F	2/2	2/2	2/1	2/1	2/1	1/0	0/0
3502	F	2/2	2/2	2/1	2/1	2/1	1/1	0/0
3503	F	2/2	2/1	1/1	1/0	1/0	0/0	0/0
Severity of Irritation - Mean Score		2/2	2/1.7	1.7/1	1.7/0.7	1.7/0.7	0.7/0.3	0/0

A. Observations: Within 1-hour post-patch removal, all 3/3/ treated sites exhibited well-defined erythema (score 2) and slight edema (score 2). The overall incidence and severity of irritation decreased gradually with time. Irritation cleared from all treated sites within 14 days.

B. Results: The PDII is 3.2.

C. Reviewer's Conclusions: In agreement with the study author; the test material is a moderate irritant and is classified as EPA Toxicity Category III.

D. Deficiencies: None.

Reviewer: Breann Hanson **Date:** August 9, 2011
Risk Manager (EPA): Bonaventure Akinlosotu, RM 10

STUDY TYPE: Dermal Sensitization – Guinea Pig; OPPTS 870.2600; OECD 406

TEST MATERIAL: Hartz Dermal Treatment (Sample #13346) (Etofenprox: 55%, Piperonyl butoxide: 10%, N-octyl bicycloheptene dicarboximide: 1%, Methoprene: 2.3%, Nylar: 1%; EPSL Reference Number 091204-1R; clear slight yellow tint liquid)

CITATION: Durando, J. (2010) Dermal Sensitization Study in Guinea Pigs (Buehler Method) of Hartz Dermal Treatment (Sample #13346). Eurofins|PSL Study No: 28785. Unpublished study prepared by Eurofins|PSL. March 5, 2010. MRID 48405801.

SPONSOR: The Hartz Mountain Corporation

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 48405801), twenty young adult male guinea pigs (weight: 355-458 g; source: Elm Hill Breeding Labs, Chelmsford, Massachusetts; strain: Hartley albino) were tested with undiluted Hartz Dermal Treatment (Sample #13346) (Etofenprox: 55%, Piperonyl butoxide: 10%, N-octyl bicycloheptene dicarboximide: 1%, Methoprene: 2.3%, Nylar: 1%; EPSL Reference Number 091204-1R; clear slight yellow tint liquid) according to the Buehler method. Two separate naïve control groups of ten males each were treated at challenge and rechallenge.

Due to higher than expected irritation scores in both the test and naïve control animals after challenge with undiluted Hartz Dermal Treatment a rechallenge was conducted using 85% and 75% w/w mixtures of the test substance in mineral oil. No "positive" dermal reactions were seen following rechallenge with either the 85% or 75% mixtures.

Based on this study, Hartz Dermal Treatment is *not* a dermal sensitizer.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary dermal sensitization study (OPPTS 870.2600; OECD 406) in the Guinea pig.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. PROCEDURE

A. Induction: The dorsal area and flanks of the animals were clipped one day prior to each treatment. For each of three successive weekly inductions, 0.4 mL of the undiluted test material was applied to the left side of each animal using an occlusive 25 mm Hill Top Chamber® and secured in place with adhesive tape wrappings for six hours. Reactions were scored 24 and 48 hours post application.

B. Challenge: Twenty-seven days after the first induction, the test animals were challenged with 0.4 mL of undiluted test material (the highest non-irritating concentration according to preliminary testing), applied to naive sites on the right side of each animal, for 6 hours using the same procedure. Reactions were scored 24 and 48 hours post application.

C. Rechallenge: Due to higher than expected irritation scores in both the test and naive control animals after challenge, it was not possible to determine if a sensitization response had occurred. It was therefore necessary to conduct a rechallenge at lower concentrations of the test substance. Seven days after the primary challenge, a rechallenge was conducted using 85% and 75% w/w mixtures of the test substance in mineral oil. Four-tenths of a millilitre of each concentration was applied to a naïve site of the right side

of each animal. An additional group of ten guinea pigs was placed on test at rechallenge. Reactions were scored 24 and 48 hours post application.

D. Naive Controls: At both challenge and rechallenge, separate "naive" groups of ten previously untreated animals were treated with 0.4 mL of undiluted test material (challenge) and an 85% and 75% w/w mixture in mineral oil (rechallenge). Reactions were scored 24 and 48 hours post application.

II. RESULTS and DISCUSSION:

A. Reactions and duration: During the induction phase of the study, very faint erythema (score 0.5) was noted at some test sites (8/20) after the third induction, only.

At primary challenge, 10/20 test sites exhibited signs of a sensitization response (erythema: score 1) at 24 hours; irritation persisted at 1/20 test sites through 48 hours. Very faint erythema was noted at all other test sites. Eight of ten naïve control sites exhibited higher than expected reactions (erythema: scores 0.5-1) at 24 hours; irritation persisted at 4/10 sites through 48 hours.

Based on the reactions noted in the control animals, a rechallenge was conducted. At test sites exposed to the 85% w/w mixture, 13/20 test sites exhibited very faint erythema (score 0.5) at 24 hours; irritation persisted at 4/20 test sites through 48 hours. At test sites exposed to the 75% w/w mixture, 10/20 test sites exhibited very faint erythema (score 0.5) at 24 hours; irritation persisted at 2/20 test sites through 48 hours. At control sites exposed to the 85% w/w mixture, 5/10 test sites exhibited very faint erythema (score 0.5) at 24 hours; irritation persisted at 1/10 naive sites through 48 hours. At naive sites exposed to the 75% w/w mixture, 3/10 test sites exhibited very faint erythema (score 0.5) at 24 hours; irritation persisted at 1/10 naive sites through 48 hours.

No "positive" responses were observed at rechallenge at either the 85% or 75% w/w mixture test/control sites.

B. Positive control: The study report included the results from a positive control study with alpha-Hexylcinnamaldehyde (EPSL Study #28478, completed December 30, 2009). This positive control study was conducted within six months of the submitted study, and the study author stated that similar induction and challenge procedures were used in both studies. The reviewer considers the results of this study appropriate.

C. Reviewer's Conclusions: In agreement with the study author, the test material is *not* a dermal sensitizer.

D. Deficiencies: None.

ACUTE TOX ONE-LINERS:

1. **DP BARCODE:** D388559
2. **PC CODES:** 128965, 067501, 057001
3. **CURRENT DATE:** August 9, 2011
4. **TEST MATERIAL:**

[a] Hartz Dermal Treatment (Sample #13346) (Etofenprox: 55%, Piperonyl butoxide: 10%, N-octyl bicycloheptene dicarboximide: 1%, Methoprene: 2.3%, Nylar: 1%; EPSL Reference Number 091204-1R; clear slight yellow tint liquid)

[b] Hartz Dermal Treatment - D (Sample #13327) (Etofenprox: 55%, Piperonyl butoxide: 10%, N-octyl bicycloheptene dicarboximide: 1%, Methoprene: 2.3%, Nylar: 1%; EPSL Reference Number 091002-2H; clear slight yellow tint liquid)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity / rat [a] Eurofins|PSL Eurofins PSL No. 28782 5/MAR/2010	48405802	LD_{50} Females > 5000 mg/kg	IV	A
Acute dermal toxicity / rat [a] Eurofins|PSL Eurofins PSL No. 28783 5/MAR/2010	48405803	LD_{50} Males> 5000 mg/kg bw LD_{50} Females> 5000 mg/kg bw LD_{50} Combined> 5000 mg/kg bw	IV	A
Acute inhalation toxicity / rat	--	--	IV	W
Primary eye irritation / rabbit [b] Eurofins|PSL Eurofins PSL No. 28363 9/DEC/2009	48405805	No comeal opacity or iritis. One hour post-instillation, 3/3 treated eyes exhibited "positive" grade conjunctivitis (redness: score 2). No "positive" grade irritation was observed at 48-hours. All treated eyes were free of irritation within 72-hours. MMTS was 9.3.	III	A
Primary dermal irritation /rabbit [a] Eurofins|PSL Eurofins PSL No. 28784 5/MAR/2010	48405804	Within 1-hours: 3/3/ sites exhibited well-defined erythema (score 2) and slight edema (score 2). Overall incidence and severity of irritation decreased with time. Irritation cleared within 14 days. PDII = 3.2.	III	A
Dermal Sensitization /guinea pig Eurofins|PSL Eurofins PSL No. 28785 5/MAR/2010	48405801	Negative.	--	A

Core Grade Key: A =Acceptable, S = Supplementary, U = Unacceptable, W = Waived